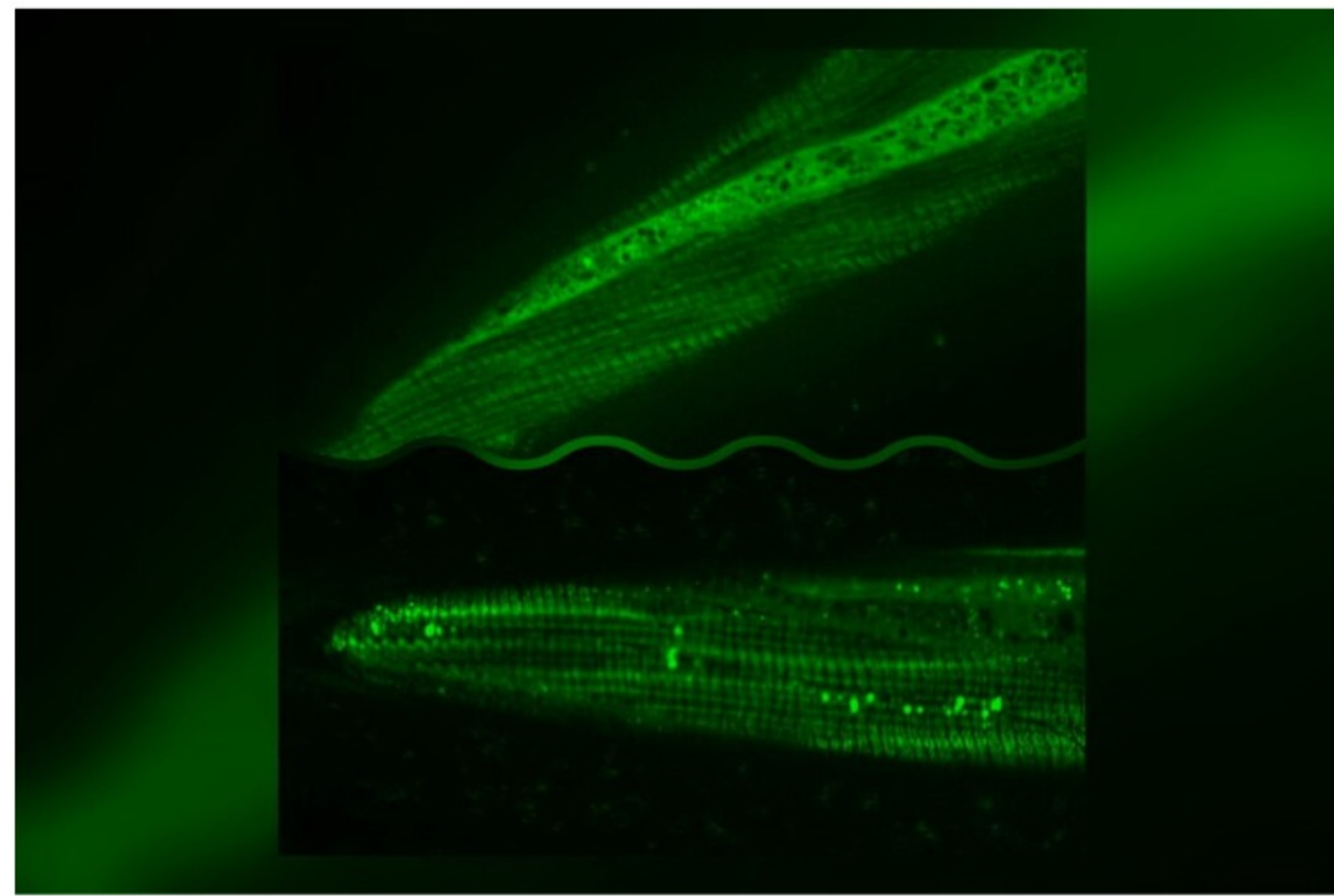


Why do we live longer when we eat less? Scientists have found the answer in nematode. Key protease that activates autophagy shows potential in antiaging therapy.

 2023-01-10 -  News

We may need not cut our diet to live longer anymore. On 0.1-cm-long nematodes, scientist have found a molecular mechanism where dietary restriction promote autophagy and delay aging. This finding has laid a clear path for determining the appropriate target of antiaging drugs.

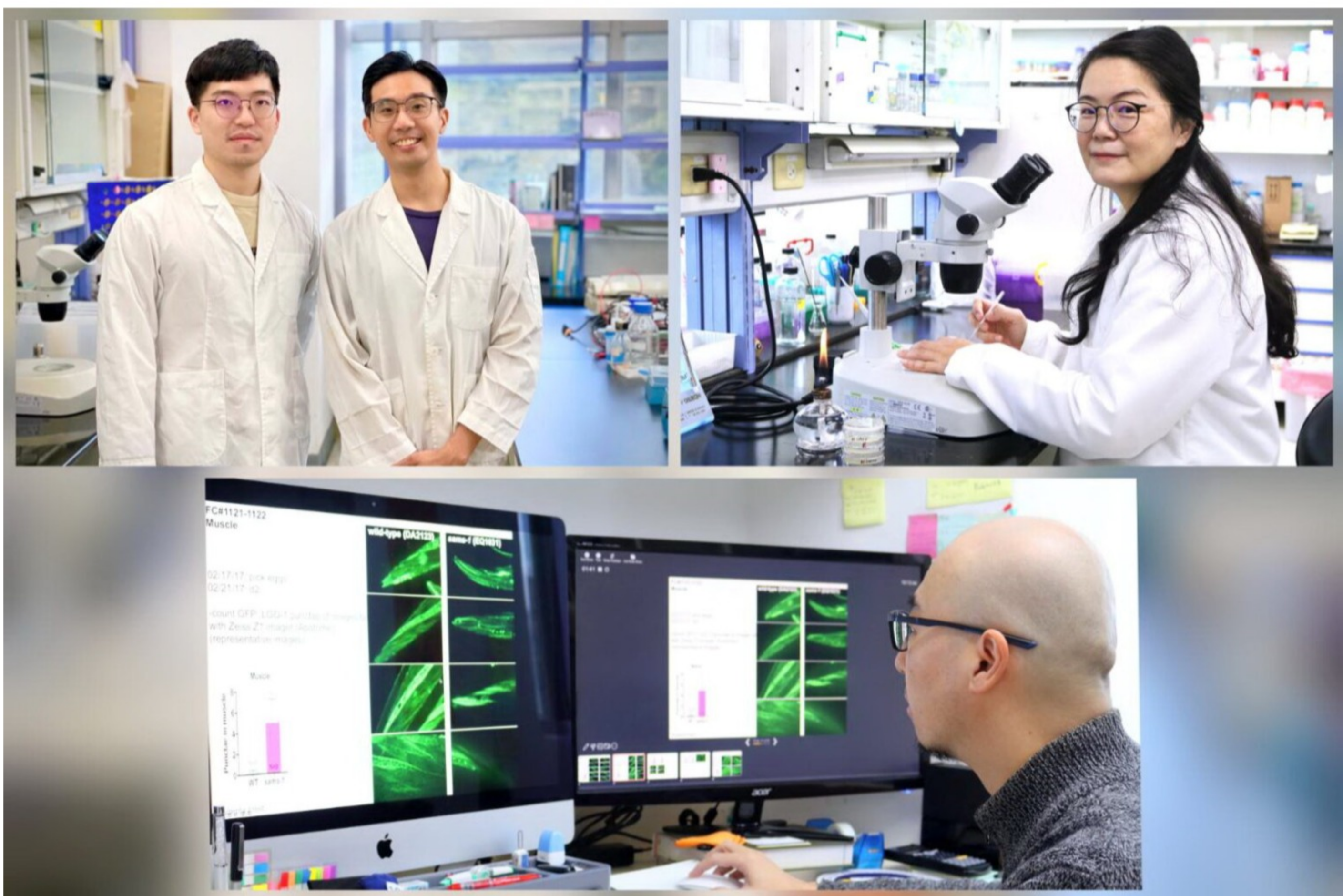
Several animal models have proven dietary restriction or calorie intake restriction in promoting autophagy and delaying aging. This is because autophagy is an inherent function of the body cells that removes damaged organelles for cell regeneration and is more obvious under certain conditions, with dietary restriction being one of them.



In recent research, scientists have found that nematodes extend their lives, which are 2 weeks on average, to 3 to 4 weeks by eating a little bit less every day. The research team observed that dietary restriction changed histonemethylation^{[1][2]} in chromosomes through two critical proteases, SAMS-1 and SET-2, thereby regulating the activity of TFEB and FOXA, two transcription factors associated with autophagy, and increasing the expression of hepatic and intestinal autophagy in nematodes.

In other words, when nematodes were fed less *Escherichia coli*, the expression of SAMS-1 was low, which affected the methylation of histones, allowing genes downstream of autophagy to be transcribed. Conversely, nematodes with a regular diet had a normal expression of SAMS-1 and exhibited limited autophagy.

Ao-Lin Hsu, the leading researchers of this research and a professor at the Institute of Biochemistry and Molecular Biology, National Yang Ming Chiao Tung University (NYCU), said that based on the prior knowledge of dietary restriction being an effective way to delay aging, this finding revealed the molecular mechanism that underlies the relationship between dietary restriction and autophagy. He also said that these findings, which revealed the critical proteins that affect aging in dieting, could help scientists determine the appropriate target of antiaging drugs and further develop aging-delaying methods that do not require dieting.



The speed of aging can be altered by environmental factors and is an inevitable part of our lives. Hsu said that an appropriate practice of dietary restriction promotes cellular repair because under a condition with insufficient resources (e.g., dietary restriction), cells prioritize repair over reproduction regarding the use of resources for survival.

In Hsu's laboratory, nematodes are the main animal used for testing. They are the top choice of animal for aging research because they are nonparasitic, live in soil, have a shorter lifespan compared with mammal animals such as mice, reproduce in large numbers within their limited lifespan, and have similar key genes to humans. This research is a joint effort between NYCU and Sanford Burnham Prebys Medical Discovery Institute. The research team also includes Tsui-Ting Ching, an associate professor at NYCU Institute of Biopharmaceutical Sciences, and Chiao-Yin Lim, the first author and a PhD student at NYCU Institute of Biochemistry and Molecular Biology. The research is published on *Autophagy*, an international journal.

[1] A histone is a protein that provides structural support for a chromosome.

[2] Methylation is a biochemical reaction. The methylation of proteins inhibits or affects gene expression and is the foundation of epigenetics.

